PCT WORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 5 : A61M 1/14, 5/142	A1	(11) International Publication Number: WO 90/06781
		(43) International Publication Date: 28 June 1990 (28.06.90)

(21) International Application Number: PCT/GB89/01486

(22) International Filing Date: 13 December 1989 (13.12.89)

(30) Priority data:
8829311.3 13 December 1988 (13.12.88) GB

(71) Applicant *(for all designated States except US)*: BIO-FLO LIMITED [GB/GB]; 32 St Andrews Road, Glasgow G41 1ST (GB).

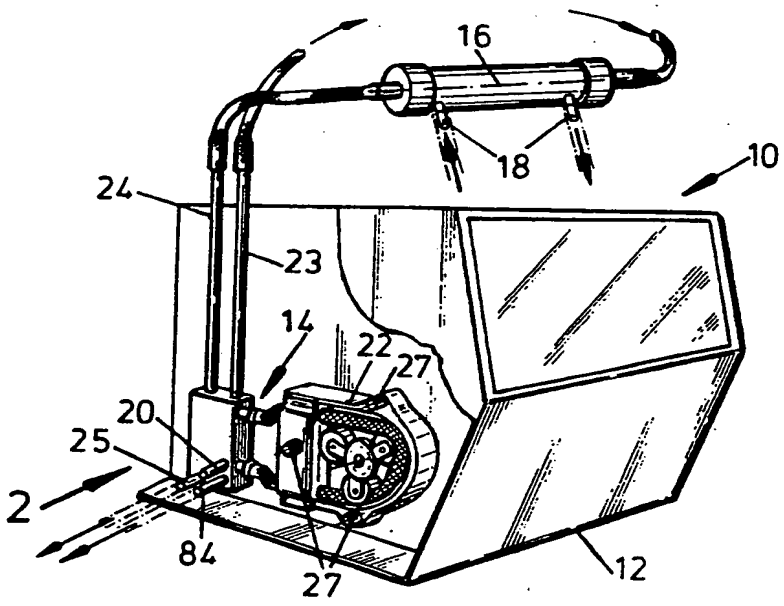
(72) Inventor; and
(75) Inventor/Applicant *(for US only)* : HOOD, Robert, Gordon [GB/GB]; "Koinonia", 10 Balgonie Woods, Paisley (GB).

(74) Agents: McCALLUM, William, Potter et al.; Cruikshank & Fairweather, 19 Royal Exchange Square, Glasgow G1 3AE (GB).

(81) Designated States: AT (European patent), AU, BE (European patent), BR, CH (European patent), DE (European patent), DK, ES (European patent), FI, FR (European patent), GB, GB (European patent), IT (European patent), JP, LU (European patent), NL (European patent), NO, SE (European patent), SU, US.

Published
With international search report.
Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.

(54) Title: FLUID FLOW CONTROL APPARATUS



(57) Abstract

A fluid flow control apparatus for use in separation and filtration is described which has a removable sterilisable/disposable element (27) which is engageable with a fixed portion (26). When engaged the flow of fluid around a fluid circuit is controlled to optimise separation. The removable element (27) may be combined with a filter unit (16) to form a unitary disposable cassette (90). Sensors (38, 40; 165, 167) can be incorporated in the apparatus for measuring fluid parameters such as pressure, viscosity and pH. Pressure sensors (165, 167; 226, 228) disposed at the filter inlet and outlet, are used to control the transmembrane pressure (TMP) to optimise filtration or separation and in one application this is used in controlling donor plasma separation.

BEST AVAILABLE COPY

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AT	Austria	ES	Spain	MG	Madagascar
AU	Australia	FI	Finland	ML	Mali
BB	Barbados	FR	France	MR	Mauritania
BE	Belgium	GA	Gabon	MW	Malawi
BF	Burkina Faso	GB	United Kingdom	NL	Netherlands
BG	Bulgaria	HU	Hungary	NO	Norway
BJ	Benin	IT	Italy	RO	Romania
BR	Brazil	JP	Japan	SD	Sudan
CA	Canada	KP	Democratic People's Republic of Korea	SE	Sweden
CF	Central African Republic			SN	Senegal
CG	Congo	KR	Republic of Korea	SU	Soviet Union
CH	Switzerland	LI	Liechtenstein	TD	Chad
CM	Cameroon	LK	Sri Lanka	TG	Togo
DE	Germany, Federal Republic of	LU	Luxembourg	US	United States of America
DK	Denmark	MC	Monaco		

FLUID FLOW CONTROL APPARATUS

The present invention relates to fluid flow control apparatus and particularly, but not exclusively, to fluid control apparatus for use in separation and filtration systems.

Fluid flow control apparatus for use in separation and filtration systems and similar fluid handling systems such as a life support system should satisfy a number of desirable criteria in addition to being efficient and relatively inexpensive. The constituent parts of the fluid control apparatus should be easily cleaned or sterilised or be disposable as this is important when using biological fluids such as blood. The apparatus should require minimal fluid volume for analyses and should accommodate sensors for monitoring various fluid parameters of the fluid. The apparatus should also permit control of fluid flow rate and pressure to suit specific separation and filtration requirements.

Existing separation and filtration equipment does not fulfil one or more of the above mentioned requirements. In particular, existing equipment does not facilitate sterilisation requiring disassembling of components and such equipment and often requiring substantial volumes of fluid for monitoring purposes. These drawbacks are particularly evident when dealing with the treatment of biological fluids, for example, blood in dialysis or life support systems. In addition, control of flow rate and

pressure is often complex in existing equipment and further reduces the sterilisability of the equipment. Thus, most existing systems tend to be aseptic rather than sterile, and this is less desirable in a clinical environment.

It is an object of the present invention to provide fluid control apparatus which obviates or mitigates at least one of the aforementioned problems.

This is achieved by a fluid flow control apparatus in which a removable sterilisable or disposable element is provided and which includes pathways and connections between other sterilisable and/or disposable items.

According to a first aspect of the present invention there is provided fluid flow control apparatus for use with a fluid handling system, said apparatus comprising a fixed portion, and a sterilisable or disposable portion removably engageable with said fixed portion, said removable portion being adapted to be coupled to pump means and to conduits in said fluid handling system and said fluid flow control apparatus having fluid pathways for permitting fluid to flow between inlet an output positions of said fluid flow control apparatus.

Preferably said removable portion includes a deformable fluid conduit, and said flow control apparatus includes flow restriction means provided by said fixed and removable portions for restricting flow in said deformable conduit when said removable portion is engaged with said

fixed portion to set the pressure in said fluid handling system. The said deformable conduit may be a separate flexible conduit adapted to be coupled between two ports on said removable portion or an integral moulded conduit disposed between two ports in said removable portion.

The fixed portion defines a recess for slidably receiving said removable portion however the removable portion can be engaged with said fixed portion by a clamp or other suitable fastener.

The fixed portion consists of two separate parts, a first guide part and a second flow restriction part in the form of a rotatable element, the first guide part defining the recess for slidably receiving the removable portion and the rotatable element for engaging with a reaction element on said removable portion so that the deformable conduit is disposed therebetween when the fixed and removable parts are engaged.

The fluid flow control apparatus conveniently includes a fluid monitoring system, said fluid monitoring system comprising a conduit disposed in said removable portion which communicates with a main fluid conduit and said conduit having an outlet port, said first guide port having a first inlet port which sealably registers with said outlet port which said removable portion is engaged, said first inlet port being the inlet of a sampling, conduit, said sampling conduit communicating with at least one aperture for receiving a sensor for measuring a fluid

parameter, said sampled fluid being passed to an outlet in said first guide port. A plurality of sensors are removably coupled to said first guide port for sensing various fluid parameters.

The fluid flow control apparatus may be used with a separation or filtration system such as a dialysis system for detoxifying blood or in a life support system.

The removable part may be made of medical grade stainless steel or sterilisable plastic. The removable part and filter unit can be combined to form a single integral cassette which is disposable or sterlisable.

The fluid flow control may be used in a dialysis system, with the apparatus adapted to receive blood to be treated, said control unit having a sterilisable removable element being coupled to peristaltic pump means and to a separate element, fluid flow restriction means coupled to said system for setting the back pressure required for dialysis, blood monitoring means coupled to said removable element for receiving a sample of blood being passed to said separation element for analysing at least one parameter of said blood, and purge means coupled to said flow control unit for being coupled to a supply of purge fluid after said dialysis to purge said blood monitoring means of blood, and control means coupled to said control unit and to said pump means and said purge means for controlling the dialysis operation and setting the blood flow rate and separation pressure.

The fluid flow control apparatus can include pressure control means for controlling the transmembrane pressure in a filtration device, the pressure control means comprising filter means having an inlet for receiving an inlet fluid to be filtered and an outlet for receiving the concentrate from said filter means, first pressure monitoring means associated with an inlet conduit for measuring the inlet pressure to said filter means, second pressure monitoring means associated with the outlet conduit for measuring the pressure of the outlet fluid, means for comparing the inlet and outlet pressures measured and flow control means coupled to said first and second pressure monitoring means to provide a comparison signal, the flow control means being responsive to the comparison signal to control the flow of fluid through said filter unit to optimise control of the transmembrane pressure and filtration.

The fluid flow control means may be a pressure switch located in the inlet conduit or it can be located in the outlet conduit.

The pressure sensors can be disposed in a bleed line of the inlet and outlet conduits so that the fluid flows past the sensors or the pressure sensors can be diaphragm pressure sensors so that there is no contact between the fluid being treated and the pressure monitoring apparatus. The transmembrane pressure arrangement can be used in a plasma separation system having a first pump at

said filter inlet, a second pump disposed at the filter outlet and a third pump disposed at the filtrate outlet, the filtrate outlet being adapted to be coupled to a reservoir of an anticoagulent substance and said filtrate output being connected to a plasma collection unit, the apparatus being arranged to separate plasma from blood donated by a patient, whereby in use, a first value of transmembrane pressure is used to actuate the first and third pumps to separate plasma and to store the separated plasma collection unit and a second value of transmembrane pressure is used to stop the first and third pumps and to actuate the second pump to return the blood to the patient.

These and other aspects of the present invention will become apparent from the following description when taken in combination with the accompanying drawings in which:-

Fig. 1 is a perspective view of a fluid separation system incorporating fluid control apparatus in accordance with an embodiment of the the present invention;

Fig. 2 is an elevational view of part of the apparatus shown in Fig.1 taken in the direction of arrow 2 and drawn to a larger scale;

Fig. 3 is a perspective and partly exploded view of parts of the apparatus shown in Fig. 1;

Fig. 4 is an elevational view of the apparatus of Fig. 3 taken in the direction of arrow 4 in Fig. 3;

Fig. 5 is a plan view of the apparatus of Fig. 3 taken in the direction of arrow 5;

Fig. 6 is a partly assembled and perspective view of the fluid control apparatus shown in Figs. 2 to 5, and

Fig 7. and 7a depicts an embodiment of a fluid flow control apparatus in which the filter and cassette are combined in a single cassette;

Fig. 8 is a diagrammatic representation of an embodiment of fluid flow control apparatus according to the present invention used in a transmembrane pressure monitoring application, and

Fig. 9 is a diagrammatic representation of a further embodiment of fluid flow control apparatus according to the present invention using transmembrane pressure monitoring to control donor plasma separation.

Reference is first made to Figs. 1 and 2 of the drawings which shows a fluid separation system generally indicated by reference numeral 10. The fluid separation system 10 is depicted in use in a dialysis system where blood is taken from a patient and filtered through a semi-permeable membrane to remove waste products in the blood before the treated blood is returned to the patient. The system consists of a fluid control unit 12 incoporating fluid flow control apparatus 14 which receives blood from a patient and which passes the blood through a hollow fibre dialysis membrane 16 which is also connected via ports 18 to a dialysate reservoir (not shown) and the filtered or treated blood is returned to the patient via the fluid flow control apparatus as will

be later described in detail.

Blood enters the apparatus 14 through main feed port 20 and is subsequently pumped through the apparatus by a 3-lobe peristaltic pump 22, along conduit 23 to the hollow fibre membrane 16. Filtered blood is returned via conduit 24 through fluid control apparatus 14 and is then returned to the patient via outlet tube 25. Parts of the fluid control unit 12, the tube in the peristaltic pump and filtration unit 16 are removable for sterilisation as will be described. The fluid control apparatus also comprises a sterilising purge system, a fluid monitoring arrangement and a transmembrane pressure monitoring system as will also be described.

The flow rate and pressure of blood in the system is controlled by pump 22 and flow control device 14. The operation of pump 22 is well known and forms no part of the invention. The pump cover can be removed using fasteners 27 to allow various parts to be replaced or sterilised if required.

Reference is now made to Figs. 3, 4 and 5 of the drawings which depict the fluid flow control apparatus 14 in greater detail. The fluid flow control apparatus 14 consists of two parts: a first main body portion, generally indicated by reference numeral 26, which remains fixed in the BIO 2000 control unit 12 and a removable cassette element 27. The main body portion 26 has two parts; a cassette guide 28 and a separate valve control

part 30. The guide 28 and valve 30 are spaced apart to define a channel 32 for slidably receiving the removable cassette element 27 in a close fitting arrangement.

The guide 28 has aseptic ports 34a, b disposed on its inner surface 36 for registering with like ports 35a, b as disposed on the outer surface 37 of cassette element 27, as best seen in Fig. 4. In the assembled condition a pressure sensor 38 and pressure switch 40 are securely fastened in the top of the guide 28 to monitor this fluid pressure.

The cassette element 27 is generally L-shaped in plan and consists of machined blocks 42 and 44 of medical grade sterilisable stainless steel which are of sufficient thickness to accommodate fluid flow channels as will be fully explained later. The cassette element 27 contains the apparatus inlet 20 and various other inlets and outlets as will also be explained. The cassette also includes an element which is part of the control valve 30. This is a fixed cylindrical boss 48 around which is located a flexible conduit 50 which connects the conduit 24 tube with the unit outlet tube 25. The main part of control value 30 includes a rotable cam 52 coupled to an electric motor 54 via gears 56 and a chain and sprocket drive 58. When the cassette element 27 is in an assembled position as in Fig. 1 or 2, the electric motor is operable by a central control unit, (not shown) within apparatus 10, to control the position of cam 52 so that the distance

between the cam 52 and boss 48 is controlled to define a 'nip' on tube 50. This nip is used to create the back pressure in the separation element or filter 16 to suit the filtration requirements of the blood.

Reference is now made to Fig. 6 of the drawings and for ease of understanding the blood flow path will be followed first. Blood to be treated is passed into the cassette element 27 via inlet 20 through internal conduit 60 (shown in broken outline) and via outlet 62 to conduit 64 of the 3-lobe peristaltic pump 22. The pumped blood is passed back to port 64 and, via internal conduit 66 the main volume of blood is passed through conduit 23 to the hollow fibre dialyser 16 for filtration as described below. A smaller volume of blood is passed along internal conduit 68 and aseptic ports 34a, 35a to internal conduit 69 disposed in the cassette element 27. The internal conduit 69 travels downwardly in portion 70 and then exits cassette 27 element via nozzle 74. To nozzle 74 is connected a conduit 76, the other end of which connects to a nozzle 78 disposed in the face 37 of cassette element 27 where it passes through aseptic ports 35b, 34b respectively to internal conduit 82 which leads to the outlet port 84.

There are drilled apertures, 86, 88 in the top of the cassette element 27 which meet with internal conduit 69 The apertures receive sensors 38, 40 so that the leading ends of the sensors are disposed within the conduit 69 for

monitoring blood parameters, in this case pH and temperature. A solenoid valve 89 is disposed in conduit 76 for controlling the start and finish of a purge operation as will be explained.

In operation, the system is connected up as shown in Fig. 1 and the system primed with blood in the usual manner. The control valve 30 is opened as is solenoid valve 89 so that a volume of blood passes through the cassette 27. Pump 22 is then started to create flow and fluid is checked in the entire system. The pump speed is then set to provide the flow conditions appropriate for separation. The control valve 30 is then adjusted to set the back pressure appropriate to the membrane for filtration requirements. During operation pressure sensor 38, monitors the fluid pressure and control pressure switch 40.

In order to stop operation, the patient is disconnected and the main valve 30 and solenoid valve 89 are opened. A purging fluid is connected to between inlet port 20 and outlet port 84 and the residue of blood is flushed out of the dialysate system and the fluid flow; control system. The pump is then stopped but the system can continue to be purged or to drain. The cassette element 27 is readily removably by sliding into and out of engagement with the fixed guide 28 and the conduit 50 can be removed to allow the cassette element 27 to be sterilised. The aseptic ports 34a,b, 35a, b, ensure that

the biological fluid is not contaminated and complies with existing safety requirements.

Various modifications can be made to the embodiment hereinbefore described without departing from the scope of the present invention. Any fluid having components which require to be filtered or separated can be used. Any other suitable form of membrane separator can be used, such as spirally wound or flat membranes as well as hollow fibre membranes. Other fluid parameters can be monitored using appropriate sensors instead of the pressure sensor and switch, for example viscosity and conductivity. The cassette can be made of sterilisable plastic instead of stainless steel and can also be disposable.

The conduit 50 need not be external but may be integral with a moulded plastic cassette but still being deformable in response to the cam to effect flow restriction. Although the fluid pathways in the removable cassette are internal it will be understood that the pathways could be external and in the form of tubes for example.

The cassette can be made as a unitary item; the filter 16 and lines can be combined with cassette 27 in an integral single unit 90 as best seen in the embodiment shown in Figs. 7 and 7a. In this case the entire cassette assembly may be disposable or sterilisable.

In addition the flow restriction means could be disposed at any suitable location rather than in the flow control

unit. For example the flow restriction means could be near or at the dialyser or the peristaltic pump. Control of the flow restriction means may be by a manual punch valve instead of the motor controlled operation. The cassette could be engaged with the fixed part other than by sliding, for example it could be placed in proximity to the fixed part and held thereat by a clamp. Furthermore the monitoring and purge system are not essential to every embodiment but only where an analysis of the fluid is required such as in the aforedescribed embodiment. Nevetherless, it is desirable to monitor certain parameters of most fluids being treated.

Reference is now made to Figure 8 of the drawings which depicts a fluid circuit generally indicated by reference number 100 for use with a BIO 2000 filtration system (Bio-flow Ltd., U.K.) whih can also be used with the embodiments of Figs. 7, 7a. In the system shown in Figure 8 a fluid conduit 152 has an inlet for receiving fluid to be treated. A three lobe roller pump 154 forces the fluid along conduit 152 and through an inlet 158 to a hollow firbe filter unit generally shown by reference numeral 160. A bleed line 162a is taken from the inlet conduit 164 so that the inlet fluid can be monitored by various sensors. In the example shown, the pressure transducer 165 and pressure switch 167 are located in the bleed line 162 for measuring the pressure parameters of the inlet fluid. The bleed line is fed to a solenoid

valve 166, the output of which is connected to a conduit 170a which, in turn, is coupled via outlet 172 to the system being treated.

The filter unit 160 has a filter output 174 which feeds outlet conduit 176 which passes through a pressure control valve, not shown in the interest of clarity, and the output from the valve constitutes the return fluid which is fed back to the source, in this example the vascular system of a patient. The outlet conduit has a bleed line 178 which is connected to a second solenoid valve 180 which has an output 182 which feeds into conduit 170 as described above. A pressure transducer 184 is located in the bleed line 178 for measuring the pressure of the filter output fluid. It will be understood that conduits 162a, 178a and 170b are located in the removable portion 14 or cassette of the BIO 2000 filtration system when these conduits are coupled via aseptic ports 163, 177 and 181 to conduits 162b, 178b and 170a respectively which are located in the fixed portion 12.

In the arrangement shown in Figure 8, the pressure switch 167 and pressure sensors 165 and 184 are located in line so that the fluid flows through and is in contact with the sensors.

With this arrangement, transmembrane pressure measurement (TMP) is achieved by monitoring the inlet pressure with transducer 165 and the outlet pressure with transducer 184. The transmembrane pressure is calculated

as the average of the inlet and outlet pressures (Po + Pi/2) less the filtrate pressure (P_f). However, filtrate or permeate pressure is low and is generally taken as zero so that the average transmembrane pressure (TMP) is deemed to be the average of the inlet and outlet pressures. The measured pressures are processed in a routine manner to provide the average pressure used to control pressure switch 167 to vary the flow through the solenoid or to affect the back pressure of the system or the signal can be used to control the valve to vary the pressure in the filter outlet conduit by varying the distance between the cam and boss and thus affect the transmembrane pressure. With this arrangement, control of the transmembrane pressure is optimised to minimise effects of gel polarisation and the like which is a process which is known to slow down filtration.

A system generally similar to that shown in Figure 8 can be used except that pressure is measured using diaphragm pressures sensors as opposed to a flow-through system which means that the fluid being filtered does not contact the monitoring sensor which maintains the sterility and the integrity of the fluid being treated.

An embodiment of the present invention set up for monitoring transmembrane pressure (TMP) will now be described in an application for controlling plasma donor separation and this is diagrammatically shown in Fig. 9

In this arrangement a vein of a patient is cannulated

with a single needle shunt 200 and the blood is pumped through 2-way line 202 by a fast 3-lobe pump 204 through fluid flow control apparatus, general indicated by reference numeral 206 through hollow fibre filter 208 and back through the apparatus 206. The filter outlet line 210 is passed through a second 3-lobe pump 212 and is coupled via 2-way line 202 to the patient. The filtrate outlet 214 of the filter is coupled via fluid line 216 to a plasma collection bag 218 and anticoagulent is pumped from a reservoir 220 by a third 3-lobe pump 222 via line 224 into line 216 to prevent the plasma from coagulating.

The fluid control apparatus 206 has inlet and output pressure sensors 226, 228 which are used to monitor the transmembrane pressure (TMP) for controlling the plasma donor separation as will be described.

In operation the system is set up as shown and pump 204 is actuated to pump blood from the patient through the system. As the blood passes through the filter it is pumped by pump 222 to bag 218 while being combined with the anticoagulent. As the blood passes to the filter retentate outlet the inlet pressure (P_i) and outlet pressure (P_o) are monitored by sensors 226, 228 respectively and the transmembrane pressure (TMP) monitored.

When the TMP reaches a first preset value pumps 204, 222 are switched off and pump 212 switched on to return the cells in the fluid retentate back to the patient via

lines 210 and 202. The TMP continues to be monitored and as the pressure falls, a second preset value is reached so that pumps 204, 222 are switched on and pump 212 is switched off to continue with further plasma separation. These procedures are repeated until sufficient plasma is separated.

It will be understood that the pressures in this application are monitored using the aforementioned pressure diaphragm sensors to avoid contact between the blood and the pressure monitoring circuitry which is an advantage of this arrangement. A further advantage is that no valves are required to control flow, this being achieved solely using the three pumps, which act as valves. Another advantage is that the total fluid line including the filter and bag is disposable. In this arrangement air bubble detectors are provided in the feed and return lines and, in the event of a bubble being detected, the whole system is shut down.

The apparatus hereinbefore described has application in other clinical areas such as life support systems as well as in the separation of substances from non-biological fluids, for example rare earth element or mineral separation. It will also be understood that the apparatus hereinbefore described can be used in different sizes, i.e. it can be scaled up to industrial plant size.

Advantages associated with the present invention are that the cassette is readily removeable to facilitate

sterilisation and the fluid volume required for monitoring is very small, being less than 40ml. The cassette can be disposable as can the entire filter and assembly in one embodiment. Also multi-point sensor access is provided to monitor various fluid parameters, and the sensors can be easily removed or replaced. In addition the pressure control for setting the filtration conditions is non-invasive and no contact is made with the fluid being treated which is important when using bioligical fluids. The transmembrane filtration/separation pressure can be readily and easily varied to suit specific filtration/separation applications and the equipment can be used with biological and non-biological fluids in various applications.

CLAIMS

1. Fluid flow control apparatus for use with a fluid handling system, said apparatus comprising a fixed portion, and a sterlisable or disposable portion removably engageable with said fixed portion, said removable portion being adapted to be coupled to pump means and to conduits in said fluid handling system and said fluid flow control apparatus having fluid pathways for permitting fluid to flow between inlet an output positions of said fluid flow control apparatus.

2. Fluid flow control apparatus as claimed in claim 1 wherein said removable portion includes a deformable fluid conduit, and said flow control apparatus includes flow restriction means provided by said fixed and removable portions for restricting flow in said deformable conduit when said removable portion is engaged with said fixed portions to set the pressure in said fluid handling system.

3. Fluid control apparatus as claimed in claim 1 or claim 2 wherein said deformable conduit is a separate flexible conduit adapted to be coupled beetween two ports on said removable portion.

4. Fluid control apparatus as claimed in claim 1 or claim 2 wherein said deformable conduit is an integral moulded conduit disposed between two ports in said removable portion.

5. Fluid control apparatus as claimed in any preceding claim wherein the fixed portion defines a recess for

slidably receiving said removable portion.

6. Fluid control apparatus as claimed in any one of claims 1 to 4 wherein the removable portion can be engaged with said fixed portion by a clamp or other suitable fastener.

7. Fluid control apparatus as claimed in any preceding system wherein the fixed portion consists of two separate parts, a first guide part and a second flow restriction part, the first guide part defining the recess for slidably receiving the removable portion and the flow restriction part for engaging with a reaction element on said removable portion so that the deformable conduit is disposed therebetween when the fixed and removable parts are engaged.

8. Fluid control apparatus as claimed in claim 7 when said flow restriction means is provided by a rotatable element which compresses said deformable conduit against a nip so as to set the pressure in said fluid handling system.

9. Fluid control apparatus as claimed in claim 8 wherein said fluid flow control apparatus includes a fluid montoring system, said fluid monitoring system comprising a conduit disposed in said removable portion which communicates with a main fluid conduit, said conduit having an outlet port, said first guide port having a first inlet port which sealably registers with said outlet port with which said removable portion is engaged, said

first inlet port being the inlet of a sampling conduit, said sampling conduit communicating with at least one aperture for receiving a sensor for measuring a fluid parameter, said sampled fluid being passed to an outlet in said first guide port.

10. Fluid control apparatus as claimed in claim 9 wherein a plurality of sensors are removably coupled to said first guide port for sensing various fluid parameters.

11. Fluid control apparatus as claimed in claim 9 or claim 10 wherein said guide port outlet is coupled via valve means and a conduit to a second inlet in said guide port, said second guide port being connected via internal conduits and third and fourth ports back to said removable portion and to an outlet purge port, the arrangement being such that purging fluid can be passed through removable portion and said first guide port when said valve is opened.

12. Fluid control apparatus as claimed in any preceding claim wherein said fluid flow control apparatus is used with a separation or filtration system.

13. Fluid control apparatus as claimed in claim 12 wherein the separation system is a dialysis system for detoxifying blood.

14. Fluid control apparatus as claimed in claim 12 wherein said fluid flow control apparatus is used with a life support system.

15. Fluid control apparatus s claimed in any one of claims 9 to 14 wherein said outlet port, said first inlet port and said third and fourth inlet and outlet ports are aseptic ports.

16. Fluid control apparatus as claimed in any one of claims 9 to 15 wherein said removable part is made of medical grade stainless steel.

17. Fluid control apparatus as claimed in any one of claims 9 to 15 wherein said removable part is made of sterilisable plastic.

18. Fluid control apparatus as claimed in any preceding claim wherein the removable part and the filter unit are combined in a single integral structure which is removably coupled to the fixed part.

19. A fluid separation or filtration system including a fluid flow control apparatus as claimed in any preceding claim adapted to be coupled to; a fluid having at least one substance to be separated therefrom, to pump means for pumping fluid around said system, and to separation means for separating said substance from said fluid, said fluid flow control unit having a removable sterilisable element with fluid pathways for permitting fluid to flow around said system.

20. A system as claimed in claim 19 including fluid flow restriction means associated with said flow control unit for setting the back pressure in said separation means.

21. A system as claimed in claim 19 or 20 including fluid

monitoring means coupled to said flow control unit for monitoring at least one fluid parameter.

22. A system as claimed in any one of claims 19 to 21 including a purge system for purging fluid from said fluid monitoring means, said purge system being coupled to said fluid flow control unit and including valve means.

23. A system as claimed in any one of claims 19 to 22 wherein the separation system is a dialysis system and the flow control unit removable sterlisable element is slidably coupled to a guide means via aseptic ports whereby a sample of blood can be passed to said monitoring system for analysis.

24. A fluid flow control apparatus as claimed in any preceding claim for use in a dialysis system and adapted to receive blood to be treated, said control apparatus having a sterlisable removable element being coupled to peristaltic pump means and to a separate element, fluid flow restriction means coupled to said apparatus for setting the back pressure required for dialysis, blood monitoring means coupled to said removable element for receiving a sample of blood being passed to said separation element for analysing at least one parameter of said blood, and purge means coupled to said flow control unit for being coupled to a supply of purge fluid after said dialysis to purge said blood monitoring means of blood, and control means coupled to said control apparatus and to said pump means and said purge means for

controlling the dialysis operation and setting the blood flow rate and separation pressure.

25. Fluid flow control apparatus as claimed in claim 1 including pressure control means for controlling the transmembrane pressure in a filtration device, the pressure control means comprising filter means having an inlet for receiving an inlet fluid to be filtered and an outlet for receiving the concentrate from said filter means, first pressure monitoring means associated with an inlet conduit for measuring the inlet pressure to said filter means, second pressure monitoring means associated with the outlet conduit for measuring the pressure of the outlet fluid, means for comparing the inlet and outlet pressures measured and flow control means coupled to said first and second pressure monitoring means to provide a comparison signal, the flow control means being responsive to the comparison signal to control the flow of fluid through said filter unit to optimise control of the transmembrane pressure and filtration.

26. Fluid flow control apparatus as claimed in claim 25 wherein the fluid flow control means is a pressure switch located in the inlet conduit.

27. Fluid flow control apparatus as claimed in claim 25 wherein the pressure switch is located in the outlet conduit.

28. Fluid flow control apparatus as claimed in any one of claims 25 to 27 wherein the pressure sensors are disposed

in a bleed line of the inlet and outlet conduits so that the fluid flows past the sensors.

29. Fluid flow control apparatus as claimed in any one of claims 25 to 27 wherein the pressure sensors are diaphragm pressure sensors so that there is no contact between the fluid being treated and the pressure monitoring apparatus.

30. Fluid flow control apparatus as claimed in any one of claims 25 to 29 wherein the first and second pressure transducers are coupled to first and second solenoid valves respectively, the outputs of which are combined within a single conduit, the valves being actuatable to purge fluid from the measurement fluid circuit.

31. Fluid flow control apparatus as claimed in any one of claims 25 to 30 having a first pump at said filter inlet, a second pump disposed at the filter outlet and a third pump disposed at the filtrate outlet, the filtrate outlet being adapted to be coupled to a reservoir of an anticoagulent substance and said filtrate output being connected to a plasma collection unit, the apparatus being arranged to separate plasma from blood donated by a patient, whereby in use, a first value of transmembrane pressure is used to actuate the first and third pumps to separate plasma and to store the separated plasma collection unit and a second value of transmembrane pressure is used to stop the first and third pumps and to actuate the second pump to return the blood to the patient.

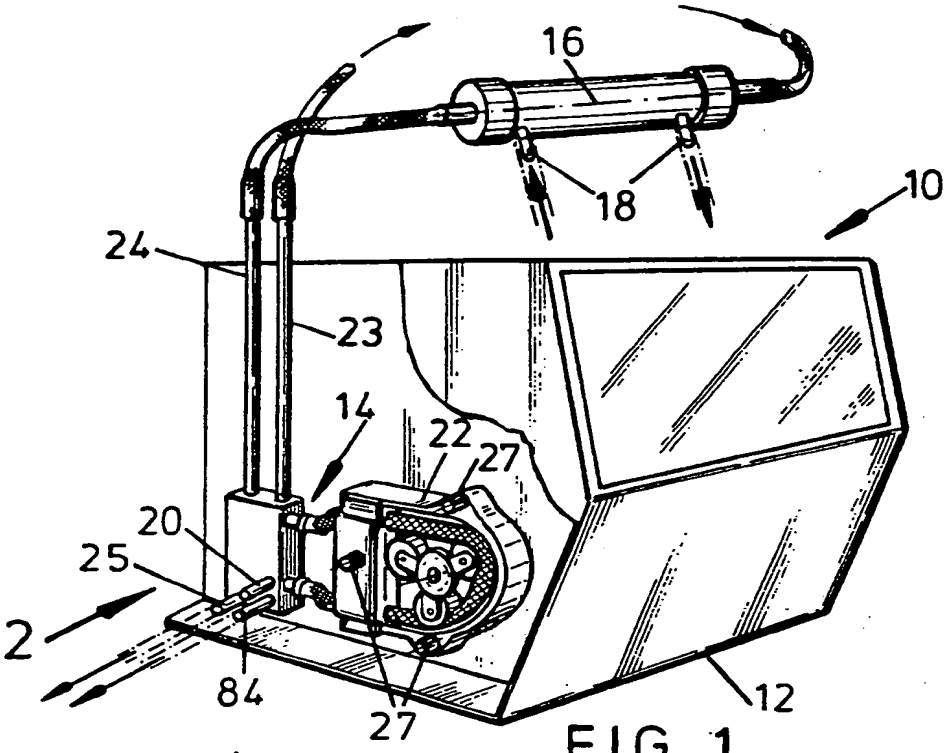


FIG. 1

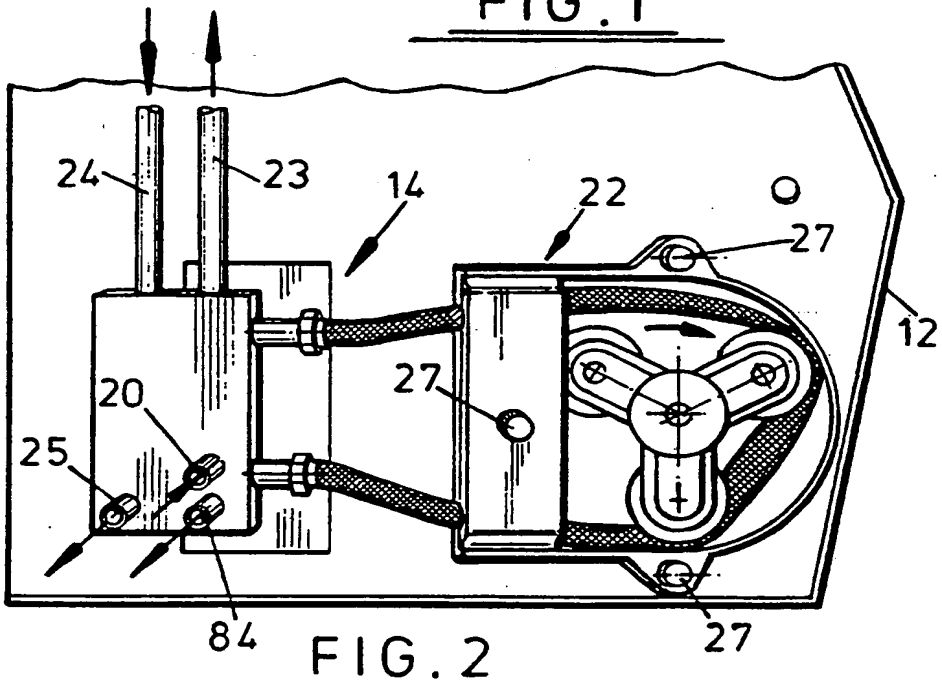


FIG. 2

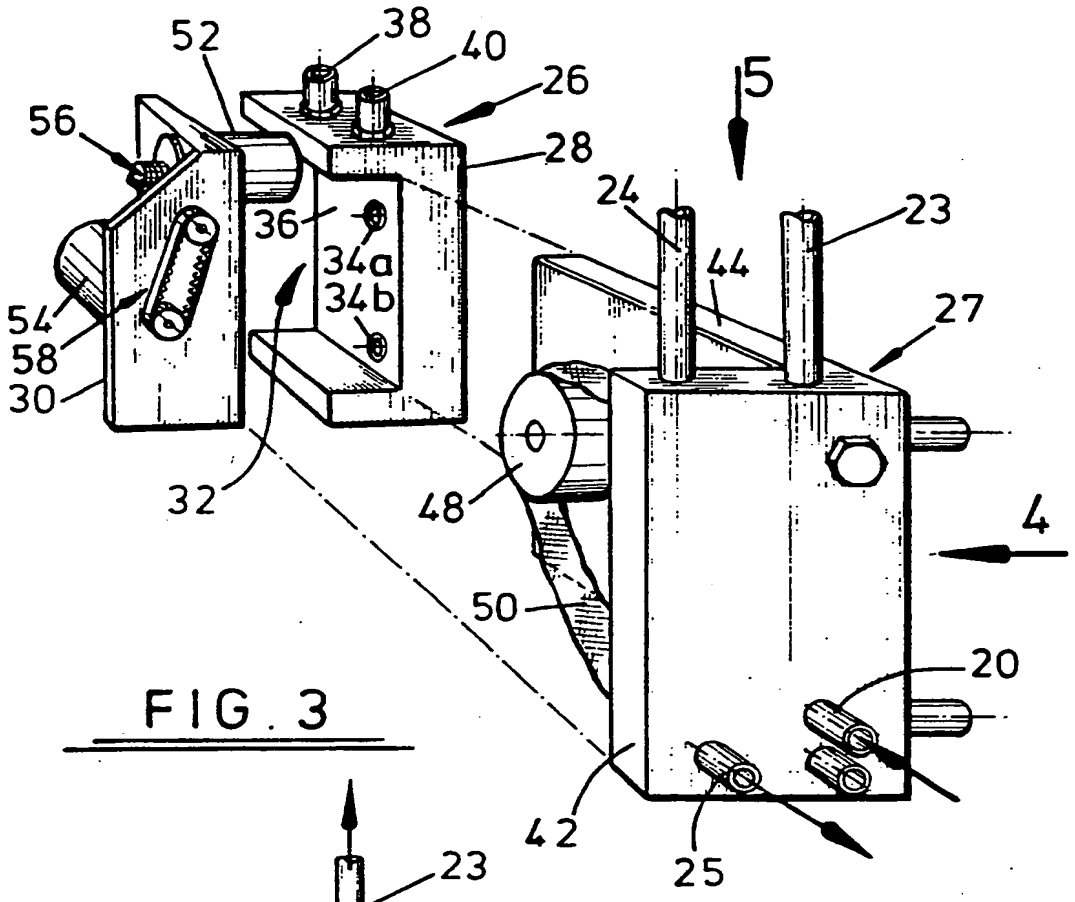

52
38
40
26
56
28
5
24
23
36
34a
34b
44
27
54
58
30
32
48
4
50
20
42
25

FIG. 3

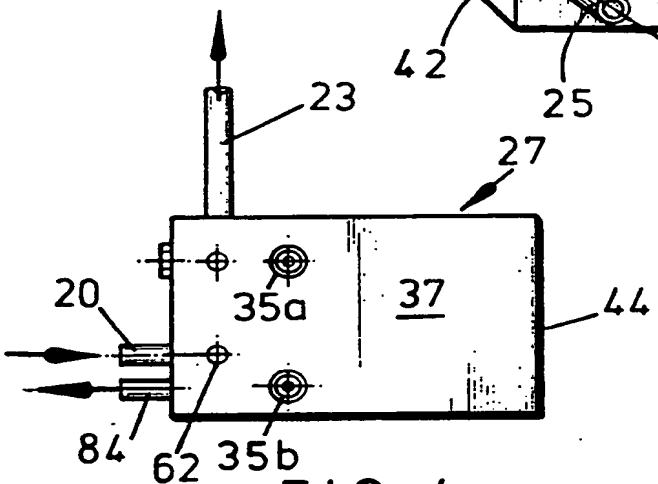

23
27
20
35a
37
44
84
62
35b

FIG. 4

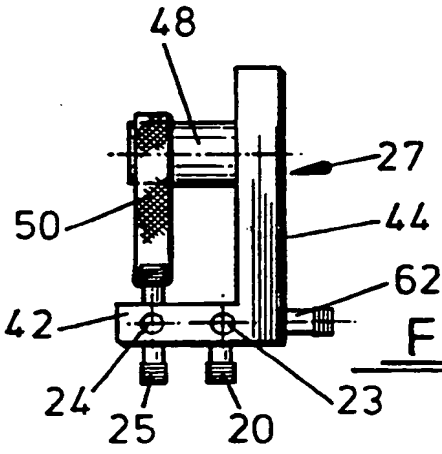

48
27
50
44
62
42
24
25
20
23

FIG. 5

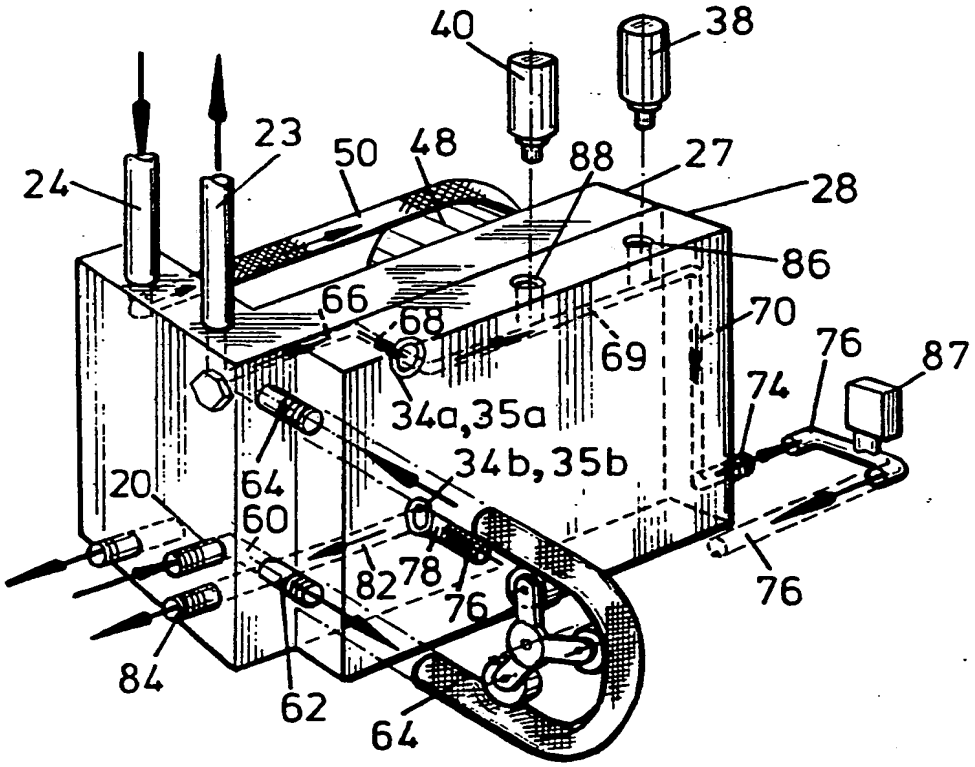

40
38
23
50
48
88
27
28
24
86
66
68
70
69
76
87
74
34a,35a
34b,35b
64
20
60
82
78
76
76
84
62
64

FIG. 6

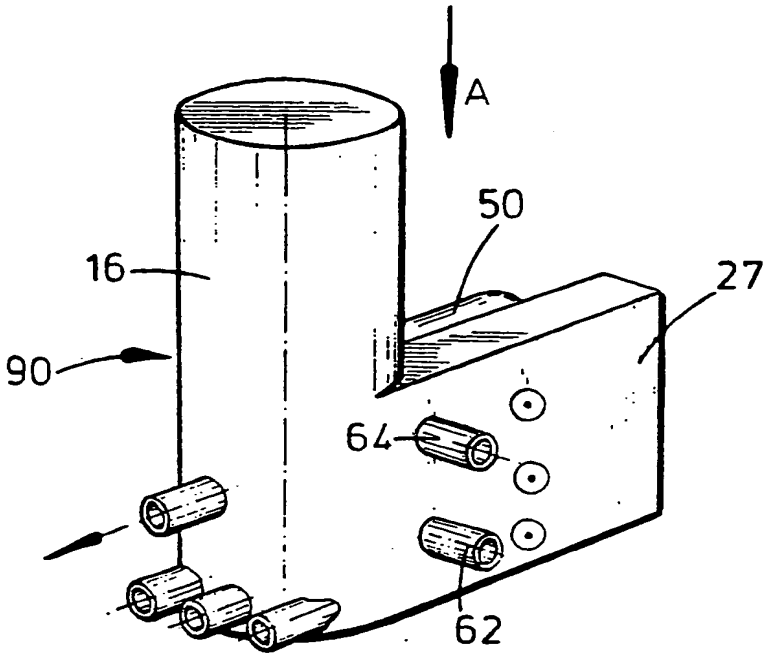


FIG. 7

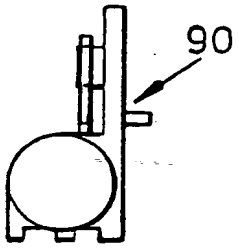


FIG. 7a

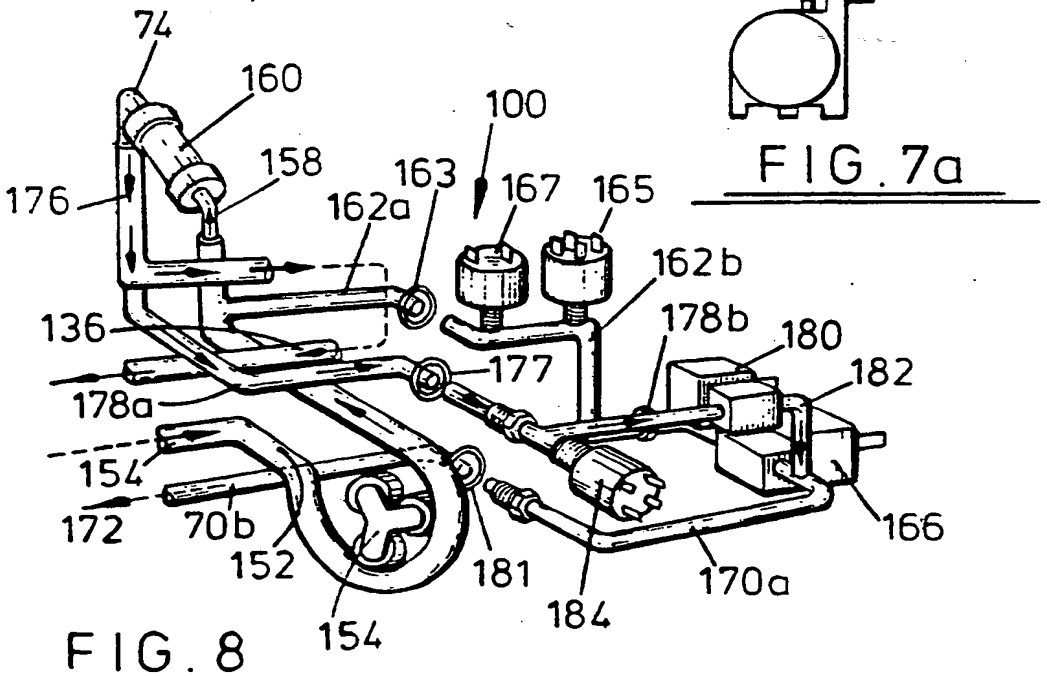


FIG. 8

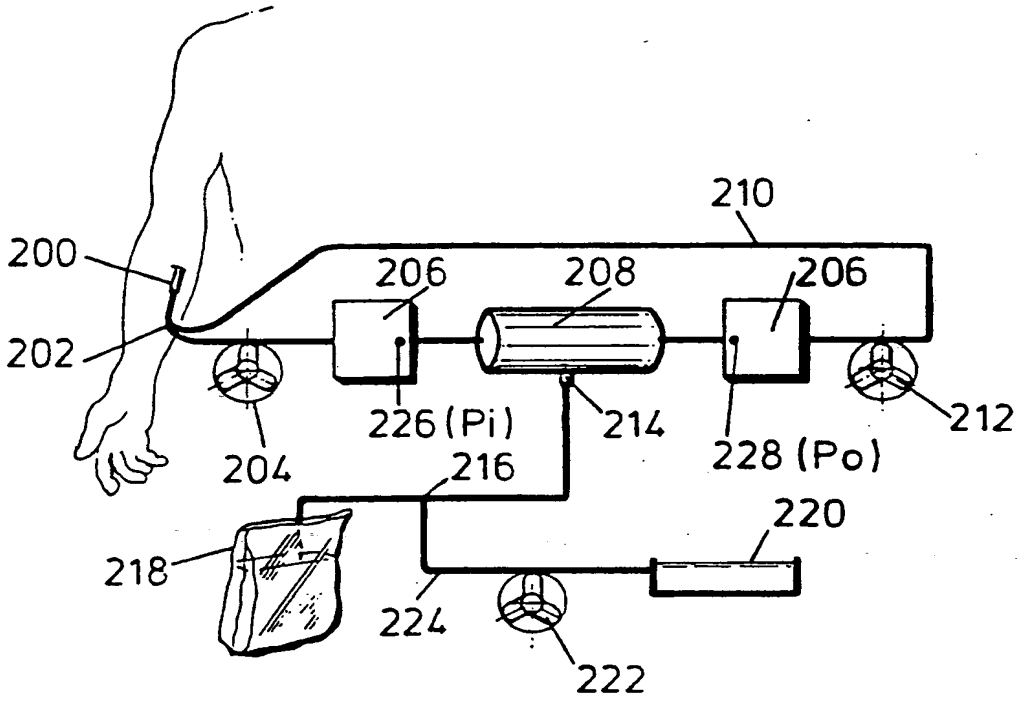

210
200
206
208
206
202
226 (Pi)
214
228 (Po)
212
204
216
220
218
224
222

FIG. 9

INTERNATIONAL SEARCH REPORT

International Application PCT/GB 89/01486

I. CLASSIFICATION OF SUBJECT MATTER (if several classification symbols apply, indicate all) *

According to International Patent Classification (IPC) or to both National Classification and IPC

IPC^5: A 61 M 1/14, A 61 M 5/142

II. FIELDS SEARCHED

Minimum Documentation Searched †

Classification System	Classification Symbols
IPC^5	A 61 M

Documentation Searched other than Minimum Documentation to the Extent that such Documents are included in the Fields Searched ‡

III. DOCUMENTS CONSIDERED TO BE RELEVANT §

Category *	Citation of Document, ¹¹ with indication, where appropriate, of the relevant passages ¹²	Relevant to Claim No. ¹³
X	US, A, 3774762 (LICHTENSTEIN) 27 November 1973 see column 3, lines 33-42; column 3, lines 64-68; column 4, lines 19-23; column 4, line 68 - column 5, line 3; column 5, lines 41-51; column 6, lines 4-7; column 7, lines 21-29; column 7, lines 39-44; column 7, lines 59-63; figure 3 --	1,2,6,12-14,17-20
X	EP, A, 0120284 (XANTHOPOULOS) 3 October 1984 see page 8, lines 7-17; page 8, lines 20-28; figures 13,14 --	1,3-5,7
X	GB, A, 2012373 (MEDICAL SCIENCES INTERNATIONAL NV) 25 July 1979 see page 2, lines 13-71, 101-115; page 4, lines 12-19; page 7, line 126 - page 8, line 12; figures 1,8-10,12	1-7

---

* Special categories of cited documents: ¹⁰

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

IV. CERTIFICATION

Date of the Actual Completion of the International Search	Date of Mailing of this International Search Report
27th march 1990	16. 05. 90
International Searching Authority	**Signature of Authorized Officer**
EUROPEAN PATENT OFFICE	M. PEIS M. Peis

Form PCT/ISA/210 (second sheet) (January 1985)

FURTHER INFORMATION CONTINUED FROM THE SECOND SHEET

V. [X] OBSERVATIONS WHERE CERTAIN CLAIMS WERE FOUND UNSEARCHABLE [1]

This international search report has not been established in respect of certain claims under Article 17(2) (a) for the following reasons:

1. [X] Claim numbers ..... because they relate to subject matter not required to be searched by this Authority, namely:

Please see additional sheet

2. [ ] Claim numbers ....., because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. [ ] Claim numbers....., because they are dependent claims and are not drafted in accordance with the second and third sentences of PCT Rule 6.4(a).

VI. [ ] OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING [2]

This International Searching Authority found multiple inventions in this international application as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims of the international application.

2. [ ] As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims of the international application for which fees were paid, specifically claims:

3. [ ] No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claim numbers:

4. [ ] As all searchable claims could be searched without effort justifying an additional fee, the International Searching Authority did not invite payment of any additional fee.

Remark on Protest

[ ] The additional search fees were accompanied by applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/210 (supplemental sheet(2))

1. INCONSISTENCIES

Claim 4: -"said deformable conduit" not mentioned in claim 1

Claim 9 and depending claims:- "said first guide port" not mentioned in preceding claims

Claim 24: "said separation element" not mentioned in "any preceding claim", only claims 12,13,23 mention "a separation system"

2. Claims not supported by description or not readily comprehensible:

Claims 15,23: " Aseptic port" not explained in the description

Claim 24, e.g. " a separation element" what kind of element ?

-"blood monitoring means for receiving a sample of blood"
-" sample of blood" never mentioned in the description.
Only mentioned in the introduction (page 4, lines 19-21)
where the phrasing is identical to the claims.

-" control means .....to optimize filtration"- obscure

ANNEX [redacted] THE INTERNATIONAL SEARCH REP[redacted]
ON INT[redacted]NATIONAL PATENT APPLICATION NO. GB 8901486
SA 33176

This annex lists the patent family members relating to the patent documents cited in the above-mentioned international search report.
The members are as contained in the European Patent Office EDP file on 09/05/90
The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US-A- 3774762	27-11-73	US-A- 3912455	14-10-75
EP-A- 0120284	03-10-84	US-A- 4537561	27-08-85
		JP-A- 59162381	13-09-84
GB-A- 2012373	25-07-79	US-A- 4187057	05-02-80
		CA-A- 1119461	09-03-82
		DE-A,C 2900743	12-07-79
		FR-A,B 2414644	10-08-79
		JP-A- 54103290	14-08-79
		SE-A- 7900223	12-07-79

This Page is Inserted by IFW Indexing and Scanning Operations and is not part of the Official Record

BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images include but are not limited to the items checked:

- ☐ BLACK BORDERS
- ☐ IMAGE CUT OFF AT TOP, BOTTOM OR SIDES
- ☐ FADED TEXT OR DRAWING
- ☑ BLURRED OR ILLEGIBLE TEXT OR DRAWING
- ☐ SKEWED/SLANTED IMAGES
- ☐ COLOR OR BLACK AND WHITE PHOTOGRAPHS
- ☐ GRAY SCALE DOCUMENTS
- ☑ LINES OR MARKS ON ORIGINAL DOCUMENT
- ☐ REFERENCE(S) OR EXHIBIT(S) SUBMITTED ARE POOR QUALITY
- ☐ OTHER: _____

IMAGES ARE BEST AVAILABLE COPY.
As rescanning these documents will not correct the image problems checked, please do not report these problems to the IFW Image Problem Mailbox.